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3				Examiner Name	Marjorie A. MORAN	320	
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1	U.S. PATENT DOCUMENTS								
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		OTHER ART - NON PATENT LITERATURE DOCUMENTS	
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MAN		R. Stoffel et al., "Thrombopoietin in Thrombocytopenic Mice: Evidence Against Regulation at the mRNA Level and for a Direct Regulatory Role of Platelets," The American Society of Hematology, Blood, vol. 87, no. 2, pp. 567-573, January 15, 1996.	
MAN		Warren S. Alexander, "Thrombopoietin and the c-Mpl receptor: insights from gene targeting," The International Journal of Biochemistry & Cell Biology, pp. 1027-1035, January 28, 1999.	
jusy		M. Miyazaki, et al., "The Relationship Between Carboplatin AUC and Serum Thrombopoietin Kinetics in Patients with Lung Cancer," 2 nd Department of Internal Medicine, Hiroshima University School of Medicine, Anti Cancer Research, vol. 19, pp. 667-670 (1999).	
justy		S. Vadhan-Raj, et al., "Stimulation of Megakaryocyte and Platelet Production by a Single Dose of Recombinant Human Thrombopoietin in Patients with Cancer," Annals of Internal Medicine, vol. 126, no. 9, pp. 673-681, May 1997.	
my		HE. Wichmann, et al., "A Mathematical Model of Thrombopoiesis in Rats," Cell Tissue Kinet, vol. 12, pp. 551-567, January 1979.	
my		L. A. Harker, et al., "Effects of megakaryocyte growth and development factor on platelet production, platelet life span, and platelet function in healthy human volunteers," The American Society of Hematology, Blood, vol. 95, no. 8, pp. 2514-2522, April 15, 2000.	
MAM		H. Mayani, et al., "Lineage Commitment in Human Hemopoiesis Involves Asymmetric Cell Division of Multipotent Progenitors and Does not Appeal to be Influenced by Cytokines," Journal of Cellular Physiology, vol. 157, pp. 579-586, 1993.	
Mary		David W. Golde, "The Stem Cell," Scientific American, pp. 36-43, December 1991.	
m		S. J. Morrison, et al., "The Biology of Hematopoietic Stem Cells," Annu. Rev. Cell Dev. Biol., vol. 11, pp. 35-71, 1995.	
jury		J. Eller, et al., "Modelling Thrombopoiesis Regulation-I; Model Description and Simulation Results," Comput. Math. Applic., vol. 14, no. 9-12, pp. 841-848, 1987.	
non		G. K. von Schulthess, et al., "Oscillating platelet counts in healthy individuals: Experimental investigation and quantitive evaluation of thrombocytopoietic feedback control," Scand J Haematol, vol. 36, pp. 473-479, March 8, 1986.	
may		L. A. Harker, et al., "Dose-Response Effects of Pegylated Human Megakaryocyte Growth and Development Factor on Platelet Production and Function in Nonhuman Primates," The American Society of Hematology, Blood, vol. 88, no. 2, pp. 511-521, July 15, 1996.	

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April 06, 2001
Zvia AGUR
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Marjorie A. MORAN
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FOREIGN PATENT DOCUMENTS									
Examiner Initials*	Cite No.1	Foreign Patent Document Country Number 4 K		Kind Code ⁵	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Translation ⁶		
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		OTHER ART - NON PATENT LITERATURE DOCUMENTS	
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WALL		P. A. Fielder, "Regulation of Thrombopoietin Levels by c-mpl-Mediated Binding to Platelets," The American Society of Hematology, Blood, vol. 87, no. 6, pp. 2154-2161, March 15, 1996.	
Mary		John E. J. Rasko et al., "Molecules in focus; The thrombopoietic factor, Mpl-ligand," The International Journal of Biochemistry & Cell Biology, vol. 30, pp. 657-660, 1998.	
· hory		F. J. de Sauvage, et al., "Physiological Regulation of Early and Late Stages of Megakaryocytopoiesis by Thrombopoietin," Departments of Molecular Biology, Cell Genetics, vol. 183, pp. 651-656, February 1996.	
Mary		F. Tacke, et al., "Endogenous serum levels of thrombopoietic cytokines in healthy whole-blood and platelet donors: implications for plateletpheresis," British Journal of Haematology, vol. 105, pp. 511-513, 1999.	
MAM		S. A. Burstein, et al., "Megakaryopoiesis and platelet formation," Williams Hematology, 5 th ed., Ch. 118, McGraw-Hill, Inc., 1995.	
MAN		R. Schofield, et al., "Self-Maintenance Capacity of CFU-S," Journal of Cellular Physiology, vol. 103, pp. 355-362, 1980.	
may		M. Rosendaal, et al., "Organization of Haemopoietic Stem Cells: The Generation-Age Hypothesis," Cell Tissue Kinet., vol. 12, pp. 17-29, 1979.	
M		A. Iliadis, et al., "Optimizing Drug Regimens in Cancer Chemotherapy by an Efficacy-Toxicity Mathematical Model," Computers and Biomedical Research, vol. 33, pp. 211-226, 2000.	
way		F. L. Pereira, et al., "A new optimization based approach to experimental combination chemotherapy," Frontiers Med. Biol. Engng., vol. 6, no. 4, pp. 257-268, 1995.	
		*Hassin Agur, "Optimizing Chemotherapy Scheduling Using Search Heuristics," pp. 2-36	
mary		Kenji Terashi, et al., "Close Association between Clearance of Recombinant Human Granulocyte Colony- Stimulating Factor (G-CSF) and G-CSF Receptor on Neutrophils in Cancer Patients," Antimicrobial Agents and Chemotherapy, vol. 43, no. 1, pp. 21-24, January 1999.	
mary		T. H. Price, et al., "Effect of Recombinant Granulocyte Colony-Stimulating Factor on Neutrophil Kenetics in Normal Young and Elderly Humans," The American Society of Hematology, vol. 88, no. 1, pp. 335-340, July 1, 1996.	
M		B. I. Lord, et al., "The kinetics of human granulopoiesis following treatment with granulocyte colony-stimulating factor in vivo," Proc. Natl. Acad. Sci. USA, vol. 86, pp. 9499-9503, December 1989.	

Examiner Signature	Mayoran	Date Considered	1/14/04
			

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Сотр	olete if Known
Application Number	09/827,229
Confirmation Number	7712
Filing Date	April 6, 2001
First Named Inventor	Zvia AGUR
Art Unit	1631
Examiner Name	Marjorie A. MORAN
Attorney Docket Number	Q63893

	U.S. PATENT DOCUMENTS									
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May	J. Y. Mary, "Normal Human Granulopoiesis Revisited. 1. Blood Data," Biomedicine & Pharmacotherapy, vol. 38, pp. 33-43, 1984.				
MAM		J. Y. Mary, "Normal Human Granulopoiesis Revisited. II. Bone Marrow Data," Biomedicine & Pharmacotherapy, vol. 38, pp. 66-77, 1984.			
many		C. Dresch, et al., "Growth fraction of myelocytes in normal human granulopoiesis," Cell Tissue Kinet. vol. 19, pp. 11-22, 1986.			
My		S. Schmitz, et al., "The effect of continuous G-CSF application in human cyclic neutropenia: a model analysis," British Journal of Haematology, vol. 90, pp. 41-47, 1995.			
May		S. Schmitz, et al., "Quantification of the cell kinetic effects of G-CSF using a model of human granulopoiesis," International Society for Experimental Hematology, Experimental Hematology, vol. 21, pp. 755-760, 1993.			
many		L. A. Harker, et al., "Regulation of Platelet Production and Function by Megakaryocyte Growth and Development Factor in Nonhuman Primates," The American Society of Hematology, no. 5, pp. 1833-1844, March 1996.			
MAN		Warren S. Alexander, "Thrombopoietin," The Walter and Eliza Hall Inst. for Medical Research, Growth Factors, vol. 17, pp. 13-24, 1999.			
My		Kenneth Kaushansky, "Thrombopoietin: The Primary Regulator of Platelet Production," The Journal of The American Society of Hematology, Blood, vol. 86, no. 2, pp. 419-431, July 15, 1995.	<u> </u>		
MAN		Saroj Vadhan-Raj, "Recombinant Human Thrombopoietin: Clinical Experience and In Vivo Biology," Seminars in Hematology, vol. 35, No. 3, pp. 261-268, July 1998.			
Mary		Laurence A. Harker, "Physiology and clinical applications of platelet growth factors," Curr Opin Hematol, vol. 6, pp. 127-134, 1999.			
MSV		Jack Levin, "Thrombopoietin Clinically Realized?," The New England Journal of Medicine, vol. 336, no. 6, pp. 1-3, February 6, 1997.			
my		G. Somlo, et al., "Recombinant Human Thrombopoietin in Combination with Granulocyte Colony-Stimulating Factor High-Dose Chemotherapy," The American Society of Hematology, Blood, vol. 93, no. 9, pp. 2798-2806, May 1, 1999.			
Mary		K. J. Neelis, et al., "The Efficacy of Single-Dose Administration of Thrombopoietin with Coadministration Myelosuppressed Rhesus Monkeys," The American Society of Hematology, Blood, vol. 90, no. 7, pp. 2565-2573, October 1, 1997.			

Examiner Signature	Mayoran	Date Considered 1/4/04

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Confirmation Number	7712	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
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First Named Inventor	Zvia AGUR	12
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Examiner Name	Marjorie A. MORA	AN On
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	FOREIGN PATENT DOCUMENTS								
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	OTHER ART - NON PATENT LITERATURE DOCUMENTS		
Examiner Initials*	Cite Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, No. 1 journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city, and/or country where published.	Translation ⁶	
100	L. J. Murray, et al., "Thrombopoietin Mobilizes Cd34+ Cell Subsets Into Peripheral Blood And Expands		
11 YUN	Multilineage Progenitors In Bone Marrow Of Cancer Patients With Normal Hematopoiesis," Experimental		
1	Hematology, vol. 26, pp. 207-216, 1998.		
	R. L. Basser, et al., "Randomized, Blinded, Placebo-Controlled Phase I Trial of Pegylated Recombinant	I	
· i.M	Human Megakaryocyte Growth and Development Factor with Filgrastim after Dose-Intensive		
m. II	Chemotherapy in Patients with Advanced Cancer," The American Society of Hematology, Blood, Vol. 89,		
• '	no. 9, pp. 3118-3128, 1997.		
	D. Zucker-Franklin, "The Ultrastructure of Megakaryocytes and Platelets," Dept. of Medicine and		
	Rheumatic Diseases Study Group, New York, The Platelets, Ch. 55, pp. 1553-1629.		
11.0	L. A. Harker, et al., "Thrombokinetics in Man," The Journal of Clinical Investigation, vol. 48, pp. 963-974,		
using	1969.		
11.00	Laurence H. Harker, "Thrombokinetics in Idiopathic Thrombocytopenic Purpura," British Journal of		
IM	Haematology, pp. 95-104, 1970.		
my	R, Sungaran, et al., "Localization and Regulation of Thrombopoietin mRNA Expression in Human Kidney,		
TIA AVII	Liver, Bone Marrow, and Spleen Using in Situ Hybridization," The American Society of Hematology,		
100,	Blood, vol. 89, no. 1, pp. 101-107, 1997.		
	Y. Nagata, et al., "Serum Thrombopoietin Level is not Regulated by Transcription but by the Total Counts		
11	of both Megakaryocytes and Platelets during Thrombocytopenia and Thrombocytosis," Tsukuba Life		
My	Science Center, Thrombosis and Haemostasis, vol. 77, pp. 808-814, 1997.	j	
	H. Nagahisa, et al., "Bone Marrow Stromal Cells Produce Thrombopoietin and Stimulate Magakaryocyte		
inani	Growth and Maturation but Suppress Proplatelet Formation," The American Society of Hematology, Blood,		
1,,,,	vol. 87, no. 4, pp. 1309-1316, February 15, 1996.		
	I. Athanassios, et al., "Comparison Between Optimata's Claims and Contemporary, 'state of the art' in		
	Optimizing of Anticancer Chemotherapy," Computers and Biomedical Research, vol. 33, pp. 211-226,)	
1	2000.		
will	Hui-Chi Hsu, et al., "Circulating Levels of Thrombopoietic and Inflammatory Cytokines in Patients with		
MY 1	Clonal and Reactive Thrombocytosis," J Lab Clin Med, vol. 134, no. 4, pp. 392-397, 1999.		

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